Ad hoc announcement pursuant to Art. 53 LR

Relief Therapeutics' Wholly Owned Subsidiary, APR Applied Pharma Research, Reports Data Published in the Peer Reviewed Journal, *Nutrients*, Indicating Additional Potential Benefits of Its Physiomimic™ Technology

- *Data In Healthy Volunteers Suggests That APR's Controlled Release Amino Acid Mix,* ***PKU GOLIKE®****, May Be Key To Reducing Catabolic Events In Patients With Phenylketonuria ("PKU"), Improving Utilization Of Amino Acids And Quality Of Life*

Geneva, Switzerland, September 21, 2021 – RELIEF THERAPEUTICS Holding SA (SIX: RLF, OTCQB: RLFTF) ("**Relief**"), a biopharmaceutical company seeking to provide patients therapeutic relief from serious diseases with high unmet need, today announced that its wholly owned subsidiary, APR Applied Pharma Research SA ("APR"), reported data published in the peer reviewed journal, *Nutrients*, indicating additional potential benefits of the company's Physiomimic™ Technology to the management of patients suffering from phenylketonuria ("PKU").

The paper, entitled, "Nitrogen Balance after the Administration of a Prolonged-Release Protein Substitute for Phenylketonuria as a Single Dose in Healthy Volunteers," provides a further evaluation of published data from APR's previously reported, randomized, controlled, single-dose crossover trial in healthy volunteers which showed that a prolonged-release amino acid (AA) mixture, formulated with Physiomimic Technology, significantly slowed down the release and reduced the peak plasma concentrations of essential AAs compared with a free AA mixture. Authors of the current paper, including Anita MacDonald, Ph.D. and Ania C. Muntau, M.D, renowned experts in the field of metabolic diseases, concluded that the controlled release amino acid mix (PKU GOLIKE®), given its ability to prolong the release of AAs, appears to be key to reducing catabolic events in patients with PKU, resulting in a more efficient utilization of AAs for protein synthesis and, therefore, an improved quality of life.

"The paper's conclusions reaffirm our belief as to the benefits of our patented Physiomimic Technology, the distinct advantages of our PKU GOLIKE® family of products, and the potential additional advantages conferred by the product's unique ability to prolong the release of AAs," stated Paolo Galfetti, Chief Executive Officer of APR and President of Relief Europe. "The Physiomimic Technology allows for a formulation of AAs which we believe leads to a physiological absorption profile more closely resembling the absorption profile of natural proteins. Based on the results published in the paper, we plan to explore

additional clinical assessments to support the benefits of AAs physiological absorption associated with PKU GOLIKE and the patented pharmaceutical Physiomimic Technology behind it."

"The strong clinical results are a testament to the potential benefits of PKU GOLIKE® as compared to non-prolonged release AA supplementation," stated Raghuram (Ram) Selvaraju, Chairman of the Board of Relief. "PKU GOLIKE® has been granted Orphan Drug Designation in the U.S. and further clinical studies on the benefits of the Physiomimic Technology will help as we pursue PKU GOLIKE® as a prescription product. In the meantime, we will focus on the commercial expansion and refinement of marketing activities to facilitate the growth of this product line in Europe."

About PKU GOLIKE

The PKU GOLIKE family of products are food for special medical purposes (FSMP) consisting of a phenylalanine-free amino acid mix in granules. Engineered with the Company's patented Physiomimic Technology platform, PKU GOLIKE® is the first prolonged-release amino acid product, characterized by a special coating that ensures a better physiological absorption of the amino acids, while also masking their unpleasant taste, odor and aftertaste.

About Phenylketonuria or PKU

PKU is a rare inherited disorder caused by a defect of the enzyme needed to break down phenylalanine, leading to a toxic buildup of phenylalanine when eating foods that contain protein or aspartame. Excessive levels of phenylalanine in the blood cause accumulation in the brain, which hampers proper brain development and results in neurophysiological dysfunction. Treatment of PKU is lifelong, requiring patients to follow a strict diet that severely limits phenylalanine (and, thus, protein) content. This necessitates supplementation of amino acid-based foods for special medical purposes (FSMP) to prevent protein deficiency and optimize metabolic control.

ABOUT RELIEF

Relief focuses primarily on clinical-stage programs based on molecules with a history of clinical testing and use in human patients or a strong scientific rationale. Relief's lead drug candidate, RLF-100™ (aviptadil), a synthetic form of Vasoactive Intestinal Peptide (VIP), is in late-stage clinical testing in the U.S. for the treatment of respiratory deficiency due to COVID-19. As part of its pipeline diversification strategy, in March 2021, Relief entered into a Collaboration and License Agreement with Acer Therapeutics for the worldwide development and commercialization of ACER-001. ACER-001 is a taste-masked and immediate release proprietary powder formulation of sodium phenylbutyrate (NaPB) for the treatment of Urea Cycle Disorders and Maple Syrup Urine Disease. In addition, Relief's recently completed acquisitions of APR Applied Pharma Research SA and AdVita Lifescience GmbH bring a diverse pipeline of marketed and development-stage programs.

RELIEF THERAPEUTICS Holding SA is listed on the SIX Swiss Exchange under the symbol RLF and quoted in the U.S. on OTCQB under the symbol RLFTF. For more information, visit www.relieftherapeutics.com. Follow us on **LinkedIn**.

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Disclaimer: This communication expressly or implicitly contains certain forward-looking statements concerning RELIEF THERAPEUTICS Holding SA. Such statements involve certain known and unknown risks, uncertainties and other factors, including: (i) whether PKU GOLIKE® provides the benefits described in the paper published in Nutrients, (ii) whether PKU GOLIKE® will be approved as a prescription product in the United States, and (iii) those risks discussed in Relief's filings with the SIX, which could cause the actual results, financial condition, performance or achievements of RELIEF THERAPEUTICS Holding SA to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. RELIEF THERAPEUTICS Holding SA is providing this communication as of this date and do not undertake to update any forward-looking statements contained herein as a result of new information, future events or otherwise.

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